Superficial acral fibromyxoma with bone involvement: description and postoperative follow-up☆

Dear Editor,

Superficial acral fibromyxoma (SAF) is a rare mesenchymal tumor with slow growth, fibroelastic consistency, and is generally painless. It mainly affects the hands and feet, particularly the periungual or subungual region. It is more common in men, with a ratio of 2:1, occurring around the age of 50.[1]

This tumor exhibits polymorphic features, making its diagnosis challenging. When located in the periungual region, it typically presents as a whitish or pinkish mass with mild hyperkeratosis and no visible vascular structures. On the other hand, when situated in the subungual region, it causes lunula deformity. In these cases, microhemorrhages and dilated linear vessels can be visualized on dermatoscopy.[2,3]

We report a case of SAF with bone involvement, detailing its dermatoscopic, histological, and evolutionary aspects.

A 71-year-old woman reports the appearance of a painless tumor on the left fourth toe with progressive growth for the past 5 years. On physical examination, she exhibited an erythematous lesion with fibroelastic consistency, crusts, telangiectasias, and a collar at the base (Fig. 1 A and B). Dermatoscopic examination revealed dilated linear vessels, brownish amorphous areas, and compact white plaques, suggestive of altered keratinization (Fig. 1 C and D).

On the radiograph, bone erosion associated with the thickening of soft tissues in the distal phalanx of the left fourth toe was evident (Fig. 2). An excisional biopsy without margins was performed for histological diagnosis.

The histopathological examination revealed dermal spindle cell proliferation amidst myxoid stroma (Fig. 3 A and B). Immunohistochemical examination showed positivity for CD34 (Fig. 3C), CD99 (Fig. 3D), and Ki67 in less than 5% of cells and negativity for 1A4, S100 and epithelial membrane antigen (EMA).

Given the clinical presentation, histopathological, and immunohistochemical aspects, SAF was diagnosed. The patient showed postoperative recovery of the nail plate and remains under outpatient follow-up due to the risk of recurrence (Fig. 4).

In approximately 36% of cases, SAF presents with erosive or lytic bone lesions.[4,5] Ultrasound examination can provide additional important information for surgical planning, such as tumor size, location, content, and the presence of vascularization on Doppler. It can also be used for monitoring recurrences.[6]

The treatment of choice is surgical excision, with a recurrence rate ranging from 10% to 24%, likely associated with incomplete resections. There are no reported cases of malig-

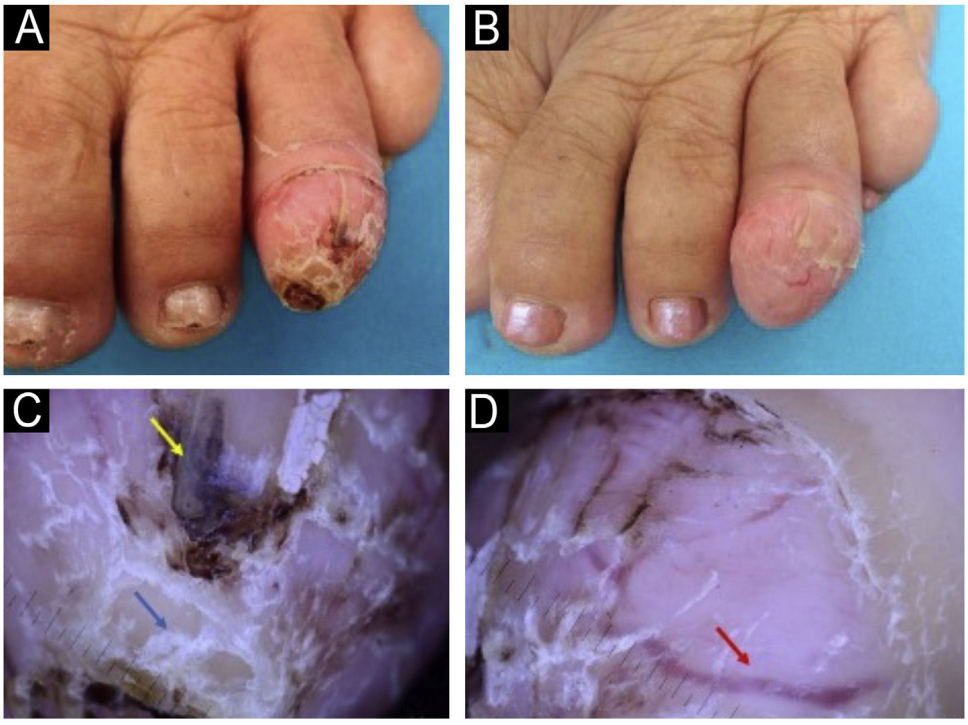

Fig. 1 (A) Keratotic tumor on the left fourth toe. (B) 14 days after photo A – Growing tumor with more evident thinning of the nail plate and telangiectasias on the surface. (C and D) Dermatoscopy 10× Presence of dilated linear vessels (red arrow), brownish amorphous areas (yellow arrow), and compact white plaques (blue arrow).

☆ Study conducted at the Clinical Hospital of the Universidade Estadual de Campinas, Campinas, SP, Brazil.

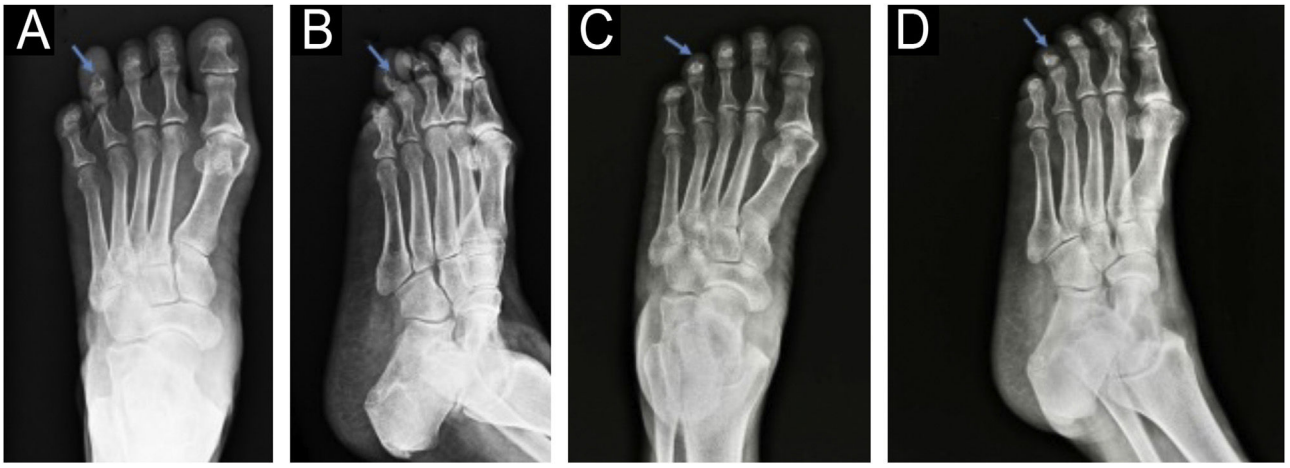

Fig. 2 Anteroposterior (A) and lateral (B) radiographs of the left foot before the surgery: increased soft tissue density and bone erosion of the distal phalanx (blue arrow), resembling a ''cup'' appearance (B). Anteroposterior (C) and lateral (D) radiographs of the left foot two months after the surgery: partial recovery of bone structure.

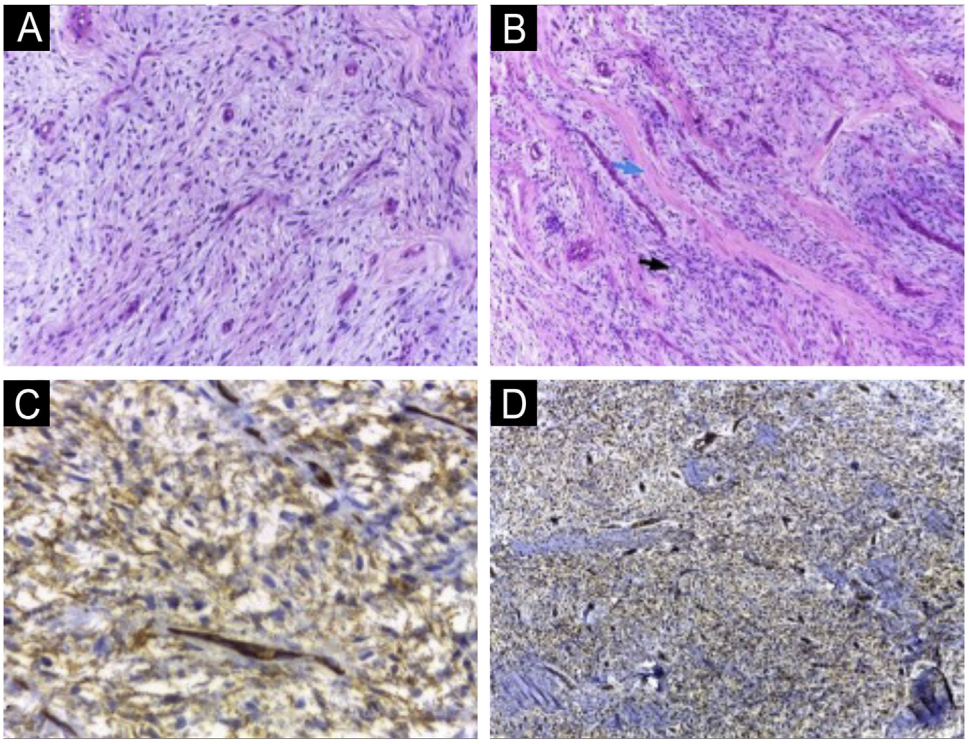

Fig. 3 (A and B) Homogeneous spindle cell proliferation amidst myxoid stroma (A); fibrosis areas (blue arrow) alternating with myxoid stroma (black arrow) (B) (Hematoxylin & eosin; 100×). Immunohistochemical study showing neoplastic cells with diffuse expression of CD34 (C) and CD99 (D) (400× and 100×, respectively).

nancy in the literature, and there is no consensus on surgical margins.[1]

The histopathological study reveals a non-encapsulated, moderately circumscribed lesion located in the dermis, which may extend into the hypodermis, fascia, or periosteal layer. There is a monomorphous proliferation of spindle cells resembling fibroblasts, embedded in a myxoid collagen stroma.[7] A characteristic finding is the presence of fibrosis areas alternating with myxoid stroma. Nuclear atypia and mitotic figures are rare.[8]

In the immunohistochemical examination, tumor cells in SAF show immunoreactivity for CD34, EMA, and CD99. In the study by Fetsch et al.,[9] which first described this tumor in 2001, positivity was reported as 91.3% for CD34, 72% for EMA, and 84.6% for CD99. Additionally, negativity is expected for cytokeratin, melanocytic markers, Smooth Muscle Actin (SMA), and desmin.[10]

The histopathological differential diagnoses include tumors with myxoid and fibromyxoid proliferation, including ungual fibroma, acquired digital fibrokeratoma, low-grade

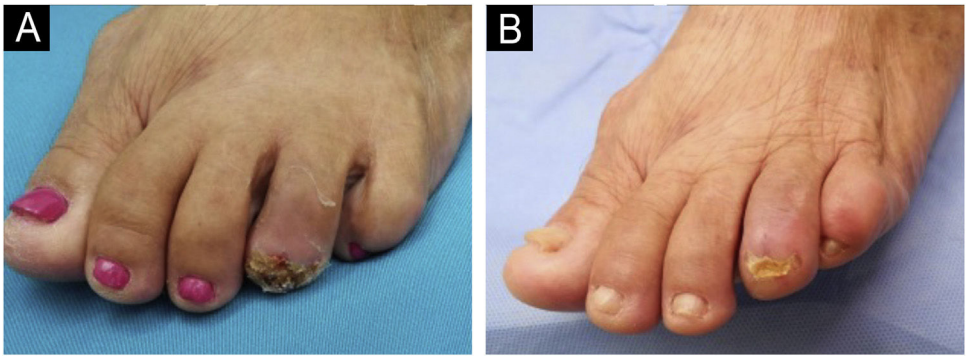

Fig. 4 (A) 30-days postoperative: presence of crusts and scaling. (B) 90-days postoperative: complete healing with apparent recovery of the nail plate.

fibromyxoid sarcoma, myxoid dermatofibrosarcoma protuberans (DFSP), angiomyxoma and myxoid neurofibroma, which will be differentiated by immunohistochemical study.

CD34-positive tumors include DFSP, neurofibroma, and angiomyxoma. Myxoid neurofibroma has a neural appearance and is positive for S100. On the other hand, DFSP may have extensive myxoid areas, mimicking SAF, with positivity for CD34 and EMA, making it a difficult differential diagnosis.[1] Peripheral areas, even if small, with the classic histological characteristics of DFSP, including a more infiltrative growth pattern, suggest this diagnosis.[9]

Superficial acral fibromyxoma (SAF) is a rare mesenchymal tumor with a challenging diagnosis, as it exhibits polymorphic clinical and dermoscopic features that resemble other digital lesions. An anatomopathological study and immunohistochemical examination are necessary for an accurate diagnosis. Despite its benign behavior, SAF can involve bone erosion and has high recurrence rates. In this context, Mohs surgery may be a good alternative for better margin control.

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Authors' contributions

Ana Carolina Baião Silva: Participated in generating data, literature review, and writing the paper.

Helena Maciel Guerra: Participated in generating data and approved the final version of this paper.

Leonardo Ávila: Participated in generating data and approved the final version of this paper.

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Renata Ferreira Magalhães: Participated in writing the paper and approved the final version of this paper.

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Conflicts of interest

None declared.

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The first case of paraneoplastic pemphigus positive for IgG autoantibodies against integrin α6☆

Dear Editor,

Paraneoplastic Pemphigus (PNP) is a rare Autoimmune Bullous Disease (AIBD) associated with neoplasm.[1] The following features can be used as references for a potential diagnosis of PNP, including (i) Mucous lesions, (ii) Histologic characteristics indicative of acantholysis or lichen planus, (iii) Positive for autoantibodies against plakin proteins, and (iv) Neoplasm.[2] In PNP, autoantibodies against diverse Basement Membrane Zone (BMZ) autoantigens, such as BP180, Laminin (LM)-332, and LMγ1, have been identified.[2,3] Given the high mortality rate of PNP, particularly in cases featuring bronchiolitis obliterans, prompt and accurate diagnosis assumes paramount importance.[2]

A 34-year-old female visited our institution on Day 0 with a one-month history of oral white patches. Histopathological analysis of a tongue biopsy revealed mucosal epithelial hyperplasia and atrophy, alongside hydropic degeneration of the basal cells and inflammatory infiltration of lymphocytes and plasma cells (Fig. 1A), indicating lichen planus. On day 118, the patient exhibited a recurrence of oral ulceration, erosion, blisters, and white stripes, accompanied by tenderness and a positive Nikolsky sign (Fig. 1B), indicative of potential AIBD. Histopathological examination of a cheek biopsy showed the features of lichen planus (data not shown). Direct immunofluorescence revealed positive intercellular staining of IgG (Fig. 1C) and C3, but not IgA and IgM (Table S1).

Indirect Immunofluorescence (IIF) using normal human skin showed negative IgG staining (Fig. 2A) but positive intercellular staining of IgA (Fig. 2B). Rat bladder IIF showed IgG staining on granular cell surface and BMZ (Fig. 2C). IIF using 1M NaCl-split normal human skin (ssIIF) showed IgG and IgA staining in both epidermal and dermal sides (Fig. 3A and 3 B). Immunoblotting (IB) of epidermal extract detected IgG and IgA autoantibodies against envoplakin and periplakin (Fig. 4A). IB of dermal extract detected IgG and IgA anti-LMγ1 autoantibody (Fig. 4B). IB of integrin α6β4 Recombinant Protein (RP) detected IgG anti-integrin α6 autoantibody (Fig. 4C). IB of LM332 RP and in house LM332 RP ELISA detected no autoantibodies against LM332 (data not shown).[4] Furthermore, ELISAs confirmed the presence of IgG autoantibodies against BP230, but not those against Desmoglein (Dsg) 1, Dsg3, BP180, or type VII collagen (Fig. 4D). On day 125, the emergency of ocular erosion was observed for the first time (data not shown). A comprehensive summary of the serological and immunofluorescence findings of this case is presented in Table S1.

Based on the aforementioned data, this patient's condition was suspected to be PNP. Subsequently, a Castleman tumor was found and surgically excised, with histopathological examination revealing follicular dendritic cell sarcoma. Additionally, bronchiolitis obliterans was confirmed via lung histopathology. After surgery, the patient's symptoms were gradually relieved with appropriate therapy. A comprehensive overview of the clinical features and treatment regimen spanning from day 0 to day 332 are summarized in Table S2.

In the present case, early AIBD serological analyses suggested the possible diagnosis of PNP, which accelerated the discovery of the Castleman tumor, confirmed the PNP diagnosis, and resulted in subsequent adjustment of therapeutic strategies. This underscores the pivotal significance of early serological diagnosis of PNP.

During the progression of the disease, this patient presented mucosal lesions without concurrent skin lesions. Except for plakin proteins, this patient's serum was also positive for autoantibodies against integrin α6, LMγ1, and BP230. To the best of our knowledge, this is the first reported case of PNP featuring anti-integrin α6 autoantibodies. Both integrin β4 and integrin α6 are considered important autoantigens for pure ocular Mucous Membrane Pemphigoid (MMP), although integrin α6 (30%) is less common than integrin β4 (60%).[5] Moreover, both IgG and IgA autoantibodies against integrin α6 and/or integrin β4 have been detected in pure ocular MMP.[5] Notably, integrin α6 is considered a principal autoantigen of oral MMP.[6] Recently, our group reported an MMP case, which presented only mucosal lesions and was positive for only anti-LMγ1autoantibodies, indicating a potential role for anti-LMγ1 autoantibodies on mucous lesion development.[7]

☆ Study conducted at the Department of Laboratory Medicine, Medical College, Dalian University, Dalian, China.